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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/018,870	04/18/2002	Hee-Yong Lee	5333-02600	8319

7590 11/05/2003

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EXAMINER	
BENNETT, RACHEL M	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 11/05/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/018,870	LEE ET AL.	
	Examiner	Art Unit	
	Rachel M. Bennett	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 May 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The examiner acknowledges receipt of the Preliminary Amendment A filed 4/18/03 and the Information Disclosure Statement filed 5/28/03.

Specification

Claim Rejections - 35 USC § 103

1. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

2. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ.459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

3. Claims 1-31 rejected under 35 U.S.C. 103(a) as being unpatentable over Supersaxo et al. (US 5470582) and further in view of Bodmer et al.

Applicants claim a process to prepare an injectable sustained release pharmaceutical composition comprising preparing biodegradable porous microspheres having accessible ionic functional groups, incorporating a biopharmaceutical into the microspheres through ionic interaction by suspending or equilibrating the microspheres in a solution comprising the

biopharmaceutical and recovering and freeze-drying the biopharmaceutical-incorporated microspheres.

Supersaxo et al. discloses a controlled release pharmaceutical composition comprising a physiologically active agent dispersed in preformed porous polymeric microparticles. The active agent concentration may be up to about 10% by weight to achieve controlled release. Each of the porous microparticles has a plurality of preformed pores into which active agent is loaded and from which the active agent is subsequently released to the environment of use. The compositions are capable of delivering physiologically effective amounts of active agent for at least 30 days. See abstract. The microparticles are polymer of polylactic, polyglycolic, or copoly(lactice/glycolic) acid and the active agent is a polypeptide. In a process for preparing the pharmaceutical compositions, the preformed porous microparticles are suspended in a solution of the active agent. After the active agent has deposited on the microparticles, they are dried, and further processed as required to remain a stable, biologically active pharmaceutical composition. See col. 2, lines 4-34. After adding the active agent, the microparticles may be dried by freeze drying. See col. 5, lines 40-43. The release rate may be controlled by co-incorporation of release rate modifying excipients and additives. Additionally, in the event the active agent is one which is deactivated by freeze-drying, a cryoprotectant may be added. Suitable excipients, additives, and cryoprotectants include proteins, such as serum albumin; carbohydrates, including simple sugars such as mannitol and sucrose and polysaccharides such as dextran, lipids such as 1,2-dipalmitoyl-sn-slycero-3-[phospho-rac-(1-glycerol)] sodium salt and surfactants such as polysorbate 80. See page 4, lines 40-54. The microparticles, which may assume a variety of shapes, generally have diameters of from about 50 to about 400 mincrons and are extensively

permeated with a network of pores into which the active agent is introduced. The active agent-containing microparticle can be easily administered in various dosage forms. For example, an injectable formulation of the microparticles may be dispersed in a suitable aqueous medium, optionally containing preservatives (e.g. methyllparaben) and/or isotonizing agents (e.g. sodium chloride, sorbitol). The dose of the controlled release composition and the selection of suitable adjuvants, carriers, and solvents will depend upon the nature and amount of physiologically active agent in the microparticles, the dosage form, the desired duration of release, the recipient animal and purpose of the administration. Supersaxo does not disclose the microparticles having accessible ionic functional groups.

Bodmer et al. disclose factors influencing the release of peptides and proteins from biodegradable parenteral depot systems. Bodmer specifically discloses design factors affecting release of octreotide and bovine serum albumin from microspheres and implants. The polymers used were biodegradable, branched poly (DL-lactide-co-glycolide-D-glucose) for microspheres. Bovine serum serves as model compound. Microspheres were produced by a modified triple-emulsion technique. The microspheres were collected by filtration, washed with water and dried under high vacuum. In vivo studies were performed with octreotide microspheres in female rabbits and in male rats. Adequate amounts of microspheres were suspended in carboxymethylcellulose solution and administered intramuscularly or subcutaneously using needles. Octreotide was encapsulated in good yields (>90%) into DL-PLG-GLU. For the evaluation of factors affecting the release properties of microspheres peptide loading, polymer molecular weight and ionic strength of the in vitro release medium were investigated. In vitro drug release increased with drug loading. See Figure 2. The release rate profiles of octreotide

from microspheres prepared with polymers of different molecular weights showed that the fraction of peptide release increased with increasing polymer molecular weight. See Figure 3. Composition and ionic strength of the in vitro release medium affected the release behavior. Osmotic effects, swelling of the devices and ionic interactions e.g. such between polymer terminal carboxylic acid groups and basic polypeptides have to be taken into account to explain the release properties of these delivery systems.

Absent unexpected results, it is the position of the examiner it would have been obvious to one of ordinary skill in the art at the time the invention was made to have modified the microparticles of Supersaxo by determining suitable ionic interactions e.g. such between polymer terminal carboxylic acid groups and basic polypeptides to determine appropriate release properties of the delivery systems as suggested by Bodmer.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rachel M. Bennett whose telephone number is (703) 308-8779. The examiner can normally be reached on Monday through Friday, 8:00 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thurman K. Page can be reached on (703) 308-2927. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

rmb

THURMAN K. PAGE
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600